How to Diagnose COVID-19 in Early Stage or Asymptomatic Patient

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ABSTRACT

The coronavirus disease 2019 (COVID-19) has rapidly progressed into a global pandemic within several months. In diagnosis, reverse transcription polymerase chain reaction (RT-PCR) is currently performed. Given the lack of sensitivity and its turnaround time, RT-PCR alone is not necessarily perfect for rapid diagnosis of COVID-19. In this article, we aim to review the typical symptoms, clinical course, manifestations and usefulness of chest CT in comparison with RT-PCR.

Keywords: Corona virus Disease; COVID-19; Chest CT

BACKGROUND

Since emerging in Wuhan, China, in late December 2019, the COVID-19 epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has progressed rapidly into a global pandemic [1]. Typical clinical symptoms of COVID-19 are fever, cough, fatigue, shortness of breath, and other respiratory tract symptoms, and in some severe cases progresses to death [2]. The ongoing pandemic of SARS-CoV-2 infections has led to 3, 557, 235 and 245,150 deaths globally as of June 6, 2020 [3].

SUBJECTIVE

The diagnosis of COVID-19 is currently performed by detecting SARS-CoV-2 RNA by RT-RT-PCR. It has been reported that the detection sensitivity is about 70%, and it takes a couple of days until the RT-PCR results are back, and therefore rapid diagnosis of COVID-19 is not necessarily easy [4].

The clinical manifestations of COVID-19 include, fever (98.6%), malaise (69.6%), dry cough (59.4%), loss of appetite (39.9%), muscle pain (34.8%), dyspnea (31.2%), sputum (26.8%), sore throat (17.4%), and diarrhea (10.1%) from a retrospective study in a single center in Wuhan [5].

In addition, smell and taste disorders (e.g. anosmia and dysgeusia) have also been reported as common symptoms in COVID-19 patients. From a retrospective study of COVID-19 patients in Italy, 34% of patients reported either a smell or taste disorder and 19% reported both symptoms [6].

There is also an observational study describing the clinical course of COVID-19 [7] (Figure 1). Dyspnea developed on day median of day 5 after onset of symptoms, and hospital admission occurred after a median of day 7 since onset of symptoms. Also, acute respiratory distress syndrome (ARDS) developed on median of day 10.5.
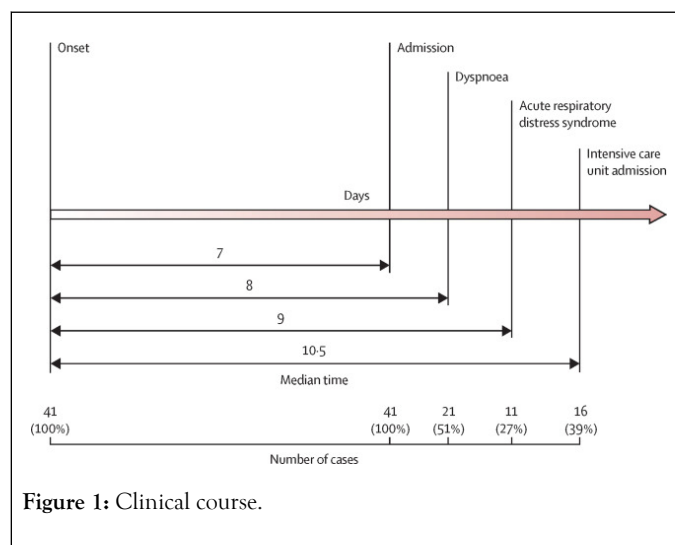

Figure 1: Clinical course.

However, it should be noted that there is a COVID-19 case report in Japan that chest CT was positive without respiratory symptoms on day 9 after onset of fever [8] (Figure 2).

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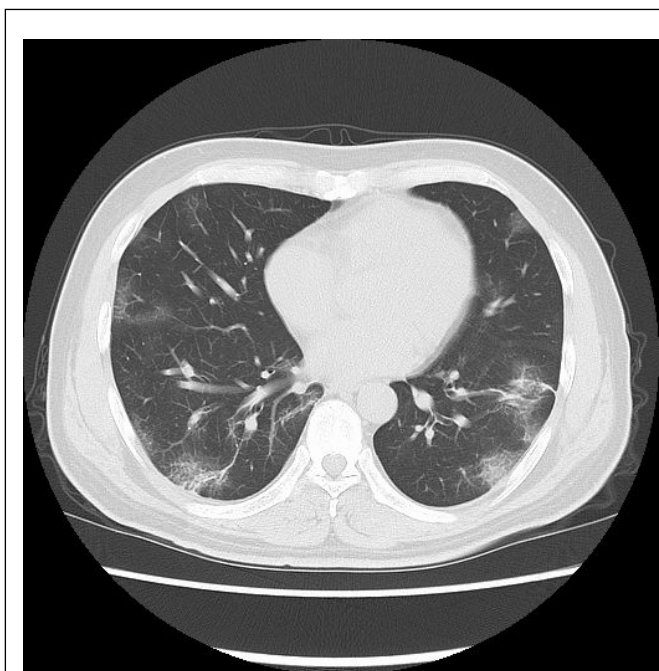
Figure 2: COVID-19 patient chest CT.

There are some studies that chest CT is useful for rapid diagnosis. Typical findings of Chest CT in COVID-19 patients reveal bilateral and peripheral ground grass opacification (GGO) with or without consolidative abnormalities [9]. As a time course of CT findings, unilateral multiple GGO turn to be bilaterally, but GGO decreases and consolidation increases over time [9].

In a study comparing chest CT from SARS-CoV-2 pneumonia in China with other causes of viral pneumonia in United States [10], SARS-CoV-2 pneumonia was more likely to have a peripheral distribution, ground grass opacification, fine reticular opacification, vascular thickening. In addition, central and peripheral distribution, air bronchogram, pleural thickening, pleural effusion, and lymphadenopathy are common in other causes of viral pneumonia.

Radiologists in United State and China joining to this study were able to distinguish SARS-CoV-2 pneumonia with high specificity but moderate sensitivity. In another observational study, of 167 patients screened, 5 (3%) had abnormal chest CT and negative result, but it became positive between 2 and 8 days later [11]. Therefore, in the case of a typical clinical course, if there are findings of COVID-19 on chest CT, we should consider patient isolation until RT-PCR is reported negative.

In another observational study of patients who underwent RT-PCR testing and chest CT for diagnose of COVID-19, abnormal finding of chest CT had a sensitivity of 97% and a specificity of 25% using RT-PCR as a reference [12]. However, in another study, 56% chest CT of COVID-19 RT-PCR positive patients reference did not show abnormal findings in the early phase (0-2 days) since onset of symptoms, but declined to 9% in 3-5 days and 4% in 6-12 days from onset, respectively [13].

Therefore, chest CT may be useful for screening. But, even with no abnormal findings, time from onset should be considered in

order to rule out COVID-19. On the other hand, there is a case report of familial cluster of infection from a asymptomatic patients who developed COVID-19 later, and another one that the viral load in the upper respiratory tract of asymptomatic patients is the same as that of symptomatic patients [14,15].

Therefore (Center for Disease Control(CDC)) suggests that self-quarantine at home for 14 days, avoiding contact with others and twice-daily temperature checks with monitoring upper respiratory symptoms for high risk potential asymptomatic patients (international traveler, those who had close contact with a patient with suspected or confirmed COVID-19) [16].

Based on the above, chest CT may be useful modality in order to diagnose asymptomatic patients and encourage them to be isolated. Several studies reported that chest CT in asymptomatic COVID-19, 50% had ground-grass opacities and the other 20% had some abnormalities [17,18].

The American College of Radiology (ACR) suggests "Usually Not Appropriate" as to whether chest CT is used for screening or diagnosis for COVID-19. The reason is that other tests such as PCR can be used for diagnosis, and the specificity of findings on chest CT is not high and overlap with other infections such as influenza, H1N1, severe acute respiratory syndrome (SARS) and middle east respiratory syndrome (MERS) [1,2].

It also discusses the issue of limited medical resources such as CT scan and medical staff, and the risk of exposure to other patients in SARS-CoV-2 in healthcare facilities. Therefore, the ACR recommends that the use of CT be limited to inpatients [19]. However, as we have suggested in this review, we believe that it is possible to prevent misdiagnosis by appropriately using CT if clinician know the limitations of chest CT. With regard to the risk of transmission to other patients, it can be reduced if precautionary measures are appropriately performed following CDC guidelines.

For the reference of the consensus statement of Radiological Society of North America (RSNA), when chest CT shows some abnormal findings incidentally, it is classified into typical, intermediate, atypical appearance, and negative for pneumonia. It is useful for radiologist to decide whether the findings on chest CT are specific for COVID-19 [20] (Table 1).

Table 1: Proposed Reporting Language for CT Findings Related to COVID-19.

Proposed Reporting Language for CT Findings Related to COVID-19			
Routine screening CT for diagnosis or exclusion of COVID-19 is currently not recommended by most professional organizations or the US Centers for Disease Control and Prevention			
COVID-19 pneumonia imaging classification	Rationale (6-11)	CT Findings*	Suggested Reporting Language

Typical appearance	Commonly reported imaging features of greater specificity for COVID-19 pneumonia.	Peripheral, bilateral, GGO* with or without consolidation or visible intralobular lines ("crazy-paving") Multifocal GGO of rounded morphology with or without consolidation or visible intralobular lines ("crazy-paving") Reverse halo sign or other findings of organizing pneumonia (seen later in the disease)	"Commonly reported imaging features of (COVID-19) pneumonia are present. Other processes such as influenza pneumonia, as can be seen with drug toxicity and connective tissue disease, can cause a similar imaging pattern." [Cov19Typ]^
Indeterminate appearance	Nonspecific imaging features of COVID-19 pneumonia.	Absence of typical features AND Presence of: Multifocal, diffuse, perihilar, or unilateral GGO with or without consolidation lacking a specific distribution and are non-rounded or non-peripheral. Few very small GGO with a non-rounded and non-peripheral distribution	"Imaging features can be seen with (COVID-19) pneumonia, though are nonspecific and can occur with a variety of infectious and noninfectious processes." [Cov19Ind]^
Atypical appearance	Uncommonly or not reported features of COVID-19 pneumonia.	Absence of typical or indeterminate features AND Presence of: Isolated lobar or segmental consolidation without GGO Discrete small nodules (centrilobular, "tree-in-bud") Lung cavitation Smooth interlobular septal thickening with pleural effusion	"Imaging features are atypical or uncommonly reported for (COVID-19) pneumonia. Alternative diagnoses should be considered." [Cov19Aty]^
Negative for pneumonia	No features of pneumonia	No CT features to suggest pneumonia.	"No CT findings present to indicate pneumonia. (Note: CT may be negative in the early stages of COVID-19.) [Cov19Neg]^

Notes:

1. Inclusion in a report of items noted in parenthesis in the Suggested Reporting Language column may depend upon clinical suspicion, local prevelance, patient status as a PUI, and local procedures regarding reporting.

2. CT is not a substitute for RT-PCR, consider testing according to local recommendations and procedures for and availability of RT-PCR

*Please see (36) for specific definitions of CT findings

*GGO= ground glass opacity

^Suggested coding for future data mining

CONCLUSION

The current COVID-19 pandemic is clearly an international public health problem. The rapid diagnosis of COVID-19 symptomatic and asymptomatic patient is sometimes difficult and challenging. It is necessary to make a comprehensive judgment based on the medical history, clinical symptoms, the results of RT-PCR and chest CT.

FUNDING

COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES

1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. N Engl J Med. 2020;382(1):1199-1207.

2. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395(10223):507-513.

3. World Health Organization. Coronavirus disease (COVID-19) pandemic. 2020.

4. Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, et al. Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR. Radiology. 2020;294(2):1-6.

5. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-1069.

6. Ralli M, Di Stadio A, Greco A,de Vincentiis M, Polimeni A. Defining the burden of olfactory dysfunction in COVID-19 patients. Eur Rev Med Pharmacol Sci. 2020;24(7):3440-3441.

7. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical Features of Patients Infected With 2019 Novel Coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.

8. Ishikawa K, Uehara Y, Matsuo T, Mori N. Pneumonia without Respiratory Symptoms. Intern Med. 2020;59(11):1469.

9. Shi H, Han X,Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological Findings From 81 Patients With COVID-19 Pneumonia in

Wuhan, China: A Descriptive Study. Lancet Infect Dis. 2020;20(4):425-434.

10. Bai HX, Hsieh B, Xiong Z, Halsey K, Choi JW, Tran TML, et al. Performance of Radiologists in Differentiating COVID-19 From Viral Pneumonia on Chest CT. Radiology. 2020;294(3):1-6.

11. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J, et al. Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing. Radiology. 2020;294(2):2-6.

12. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology. 2020;294(2):1-7.

13. Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, et al. Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection. Radiology. 2020;295(3):5-10.

14. Yu P, Zhu J, Zhang Z, Han Y. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. J Infect Dis. 2020;221(11):1757-1761.

15. Chan JFW, Yuan S, Kok KH, To KKW, Chu H, Yang J, et al. A Familial Cluster of Pneumonia Associated With the 2019 Novel Coronavirus Indicating Person-To-Person Transmission: A Study of a Family Cluster. Lancet. 2020;395(10223):514-523.

16. Centers for Disease Control and Prevention. Public Health Guidance for Community-Related Exposure:Coronavirus Disease 2019 (COVID-19). 2020.

17. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, et al. Clinical Characteristics of 24 Asymptomatic Infections With COVID-19 Screened Among Close Contacts in Nanjing, China. Sci China Life Sci. 2020;63(5):706-711.

18. Inui S, Fujikawa A, Jitsu M, Kunishima N, Watanabe S, Suzuki Y, et al. Chest CT Findings in Cases from the Cruise Ship "Diamond Princess" with Coronavirus Disease 2019 (COVID-19). Radiology Cardiothoracic Imaging. 2020;2(2):2-10.

19. American College of Radiology. ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection. 2020.

20. Simpson S, Kay FU, Abbara S, Bhalla S, Chung JH, Chung M, et al. Radiological Society of North America Expert Consensus Statement on Reporting Chest CT Findings Related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. Radiology Cardiothoracic Imaging. 2020;2(2):6-15.